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14	Postle, K., et al., (1984) "Nucleotide s	sequence of the repressor	gene of the 1445 2 pp. 4849-4863;
BN	Postle, K., et al., (1984) "Nucleotide s resistance determinant", Nucleic Acid	d Research, Vol. 12, No. 11	-1 [1
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1111	Unger, B., et al., (1984) "Nucleotide	sequence of the gene, pro	e-gene-repressor", Gene, Vol. 31,
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	Waters, S.H, et al., (1983) "The tell nucleotide sequence analysis", Nu	tracycline resistance determined Posearch, Vol.	11, No. 17, pp. 6089-6105,
BQ	nucleotide sequence analysis", Nu	icleic Acid Resourch	
1 11	1 1	il - a guance	e of the Tn10 encoded tetracycline
	Hillen, W., and Schollmeier, K., (1 resistance gene", <i>Nucleic Acid Re</i>	983) "Nucleotide Sequence	525-539;
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	Damke, H. et a	al.,"Inducti	ion of Mutant Dyna	min Specifically Bl	ocks Endo	ocytic Coated \	/esicle
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BZ	induces Apopto	osis", <i>⊵ivie</i>	30 <i>Journal</i> , Vol. 14	l (19), pp. 4662-46	75 (1995)		
	Investigation, V	al.," l etra /ol. 93. pp	cycline-regulated (_ 1864-1868 (1994	Cardiac Gene Expr	ession in '	Vivo", <i>Journal</i> d	of Clinical
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Haase, S. et al., "Transcription Inhibits the Replication of Autonomously Replicating Plasmids i Human Cells", *Molecular and Cellular Biology*, Vol. 14 (4), pp. 2516-2524 (1994);

Hennighausen, L. et al., "Conditional Gene Expression in Secretory Tissues and Skin of Transgenic Mice Using the MMTV-LTR and the Tetracycline Responsive System", *Journal of Cellular Biochemistry*, Vol. 59, pp. 463-472 (1995);

Maheswaran, S. et al., "The WT1 Gene Product Stabilizes p53 and Inhibits p53-mediated Apoptosis". Genes & Development Vol. 9, pp. 3443-3456 (4995)

Apoptosis", Genes & Development, Vol. 9, pp. 2143-2156 (1995);

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ELI		UBLICATIONS CITED BY APPLICANT lse several sheets if necessary)	Bujard, H., Gossen, M., S	alfeld, J. and Voss, J					
R 89.	0 1		March 30, 1999	1643— 1632—					
, , ,	N. C.	OTHERS (including Author, Title, D	Date, Pertinent Pages, Etc.)						
EMP		Miller, K. et al., "The Function of Inducible Experimental Cell Research, Vol. 218, pp	o. 144-150 (1995);						
	CG	Passman, R. et al., "Regulated Expression Journal of Clinical Invest., Vol. 94, pp. 24.	n of Foreign Genes in Vivo A 21-2425 (1994);	After Germline Transfer",					
	СН	Resnitzky, D. et al., "Acceleration of the G1/S Phase Transition by Expression of Cyclins D1 abd E with an Inducible System", <i>Molecular and Cellular Biology</i> , Vol. 14 (3), pp. 1669-1679 (1994);							
$\overline{\mathbf{I}}$	CI	Shan, B. et al.,"Deregulated Expression of	Shan, B. et al., "Deregulated Expression of E2F-1 Induces S-Phase Entry and Leads to Apoptosis", <i>Molecular and Cellular Biology</i> , Vol. 14 (12), pp. 8166-8173 (1994);						
	Cl	Sopher, B. et al., "Cytotoxicity Mediated by Derivative of the β-amyloid Precursor Pro (1994);	y Conditional Expression of	a Carboxyl-terminal					
	СК	Wimmel, A. et al.,"Inducible Acceleration Expression of Human cyclin E", Oncogen	of G1 Progression Through e, Vol. 9, pp. 995-997 (1994)	Tetracycline-regulated);					
3	CL	Wu, Z. et al., "Conditional Ectopic Express Stimulates Adipogenesis", Genes & Deve	sion of C/EBP β in NIH-3T3 Colopment, Vol. 9, pp. 2350-23	ells Induces PPARγ and 663 (1995);					

Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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		OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)					
M	cs	Ackland-Berglund, C.E. and Leib, D.A. (1995) BioTechniques 19:216-217;					
	СТ	Ackland-Berglund, C.E. and Leib, D.A. (1995) "Efficacy of Tetracycline-Controlled Gene Expression Is Influenced by Cell Type" <i>BioTechniques</i> 18(2):196-200;					
	CU	Agarwal, M.L. et al., "p53 Controls Both the G ₂ /M and the G ₁ Cell Cycle Checkpoints and Mediates Reversible Growth Arrest in Human fibroblasts," <i>Proceedings of the National Academy of Science</i> , Sci. USA, 92: pp. 8493-8497 (1995);					
	cv	Altschmied, L. et al., (1988) "A threonine to alanine exchange at position 40 of Tet repressor alters the recognition of the sixth base pair of <i>tet</i> operator from GC to AT", <i>The EMBO Journal</i> , 7(12):4011-4017;					
	cw	Baniahmad, A. et al. (1992) "A Transferable Silencing Domain Is Present In the Thyroid Hormone Receptor, In the v-erbA Oncogene Product and In the Retinoic Acid Receptor" <i>The EMBO Journal</i> 11(3):1015-1023;					
	СХ	Baumeister, R. et al.(1992)"Tet Repressor <i>Tet</i> Operator Interactions Derived From Mutants With New Recognition Specificities", <i>Structural Tools For The Analysis Of Proten-Nucleic Acid Complexes Advances In Life Sciences</i> , Birkhauser, Basel ;Boston, pp. 175-183;					
	CY	Baumeister, R. et al.(1992)"Contacts Between Tet Repressor And <i>Tet</i> Operator Revealed By New Recognition Specificities Of Single Amino Acids Replacement Mutants", <i>Journal Of Molecular Boiology</i> , Vol. 226, pp. 1257-1270;					
	CZ	Baumeister, R. et al.(1992)"Functional Roles Of Amino Acid Residues Involved In Forming THE.Alphahelix-turnalphahelix operator DNA Binding Motif Of Tet repressor From Tn10", <i>Proteins: Structure, Function, and Genetics</i> , Vol. 14(2), pp. 168-177;					
A C	DA	Bradley, A., (1992)"Modifying The Mouse: Design And Desire", <i>Biotechnology</i> , Vol. 10, pp. 534-539;					
Examiner	•	Date Considered Stri N					

*EXAMINER:

Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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	7-80	U.S. DEPARTMENT OF COMMERC PATENT AND TRADEMARK OFFICE	BBI-013C3CN2	SERIAL NO. 09/281,674	
PE	LIST C	OF PUBLICATIONS CITED BY APPLICANT (Use several sheets if necessary)	Bujard, H., Gossen, M., Salfeld, J. and Voss, J.		
`	,		03/30/1999	1643 \b & 2	
OCT U		OTHERS (including Author, Title			
Tre or a	AL SERVICE SERVICE	Cayrol, C. et al. "Identification of Cellula Zta: Activation of Transforming Growth Virology, 69, No. 7, pp. 4206-4212, (198	Factor βigh3 (TGF-βigh3) 95);	and TGF-β1", Journal of	
L	DC	Chen, Y.Q. et al. "Tumor Suppression b (1995);	y p21 ^{VVAF11} ", Cancer Re	search, <u>55</u> , pp. 4536-4539,	
	DD	Coghlan, A. "Gene dream fades away"	New Scientist 148, pp. 14-	15, (1995);	
	DE	Cowell, "Repression versus activation in Biochemical Sciences, 19:1, 38-42 (199		ription," <i>Trends in</i>	
	DF	Crystal, R.G. "Transfer of Genes to Hun Science 270, pp. 404-410 (1995);	nans: Early Lessons and C	bstacles to Success",	
	DG	Daddona et al., "Human Adenosine Dea	nminase." J. Biol. Chem. 2	59: 12101-12106(1984);	
	DH	Deuschle et al., "Tetracycline-reversible 1907-1914 (1995);	silencing of eukaryotic pro	omoters," Mol. Cell. Biol., 15:4,	
	DI	Ebert, K.M. et al. (1988) "A Moloney ML Active Somatotropin in a Transgenic Pig			
	DJ	Fields, S. et al (1989) "A novel genetic s 245-246;	system to detect protein-pro	otein interactions" Nature 340:	
	DK	Figge, J., et al., (1988) "Stringent Regula Transferase Genes by <i>E. coli lac</i> Repres			
	DL	Frankel, F.D. et al (1988) "Tat Protein fro Linked Dimer" <i>Science</i> 240: 70-73;	om Human Immunodeficier	ncy Virus Forms a Metal-	
Π	DM	Furth P. (1994) "Temporal Control of Ge Responsive Promoter" <i>Proc. Natl. Acad</i>		nic Mice By A Tetracycline-	
	DN	Gatz et al. "Stringent repression and hor CaMV 35S promoter in intact transgenic (1992);	tobacco plants," The Plan	t Journal, 2:3, 397-404	
	DO	Gatz, C. et al. "Regulation of a modified repressor in Transgenic Tobacco" <i>Mol.</i> (
	DP	Gjetting, T. et al. "Regulated Expression Carcinoma Cells Restores Cyclin D1 Ex Seyler, 376, pp. 441-446 (1995);	of the Retinoblastoma Sus	sceptibility Gene in Mammary	
\prod	DQ	Gossen M. and B. Hermann (1993) "Anh Controlled Gene Expression Systems In 4412;			

ExaminerDS

Gossen, M., et al., (1993) "Control of gene activity in higher eukaryotic cells by prokaryotic regulatory elements", *TIBS* 18(12):471-475; **Date Considered**

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*EXAMINER:

Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

11 11 11	3	00/00/1000						
		OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)						
CV.	MS.	Gossen et al., "Exploiting prokaryotic elements for the control of gene activity in higher eukaryotics," Keystone Symposium on Gene Therapy and Molecular Medicine, Steamboat Springs, Colorado, <i>Journal of Cellular Biochemistry</i> , Supplement 0 (21A), Abstract no. C6-220, 355 (1995);						
	DT	Gossen et al. (1994) "Inducible Gene Expression Systems For Higher Eukaryotic Cells" <i>Current Opinion in Biotechnology</i> 5:516-520;						
	DU	Gossen et al., "Transcriptional activation by tetracyclines in mammalian cells," <i>Science</i> , 268:5218, 1766-1769 (1995);						
	DV	Gunzburg, W.H. and Salmons, B. "Virus vector design in gene therapy", <i>Molecular Medicine Today</i> 1, pp. 410-417, (1995);						
	DW	Hammer, R.E. et al. (1986) "Genetic Engineering of Mammalian Embryos." J. Anim. Sci. 63: 269-278; Hecht, B., et al., (1993) "Noninducible Tet Repressor Mutations Map from the Operator Motif to the C Terminus", <i>Journal of Bacteriology</i> 175(4);						
	DX							
	DY	Herschbach B. and A. Johnson (1993) "Transcriptional Repression In Eukaryotes" <i>Annu. Rev. Cell Biol.</i> 9:479-509;						
	DZ	Hinrichs, W., et al., (1994) "Structure of the Tet Repressor-Tetracycline Complex and Regulation of Antibiotic Resistance", <i>Science</i> 264:418-420; Howe, J.R. et al., (1995) "The Responsiveness of a Tetracycline-Sensitive Expression System Differs in Different Cell Lines", <i>The Journal of Biological Chemistry</i> , 270, No. 23, pp. 14168-14174;						
	EA							
	ЕВ	Houdebine, LM. (1994)"Production of Parmaceutical Proteins From Transgenic Animals", Journal Of Biotechnology Vol. 34, pp. 269-287;						
	EC	Kao, C.C., et al. (1990) "Cloning of a Transcriptionally Active Human TATA Binding Factor" Science 248: 1646-1650;						
	ED	Kappel, C.A., et al., (1992)"Regulating Gene Expression In Transgenic Animals", <i>Current Opinion In Biotechnology</i> , Vol. 3, pp. 548-553;						
	EF	Krimpenfort, P. et al. "Generation of Transgenic Dairy Cattle Using 'in vitro' Embryo Production." BIO/Technology 9, pp. 844-847 (1991);						
	EG	Landschulz, W.H. et al. (1989) "The DNA Binding Domain of the Rat Liver Nuclear Protein C/EBP is Bipartite" Science 243: 1681-1688;						
	EH	Liang et al., (1995)"Enhanced and switchable expression systems for gene-transfer," Keystone Symposium on Gene Therapy and Molecular Medicine, Steamboat Springs, Colorado, <i>Journal of Cellular Biochemistry</i> , Supplement 0 (21A), Abstract no. C6-220, 379;						
	EI	Licht, J. et al. (1990) "Drosophila Krüppel Protein is a Transcriptional Repressor" <i>Nature</i> 346:76-79;						
	EJ	Marshall, E. "Gene Therapy's Growing Pains" Science 269, pp. 1050-1055 (1995);						
(e)	EK	Mastrelangelo et al "Gene Terapy for Human Cancer: An Essay for Clinicians" Seminars in Oncology 23 (1), pp. 4-21 (1996);						
Èxamir	ner	Date Considered 5/21 N						
*EXAN	IINER:	Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant						

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		<u> </u>	OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)		
	. «		McKnight, S.L., (1984) "The Distal Transcription Signals of the Herpesvirus tk Gene Share a		
2 TEN	٧.		Common Hexanucleotide Control Sequence" Cell 37: 253-262;		
C(V EM			Mendez, B. et al. "Heterogeneity of tetracycline resistance determinants" <i>Plasmid</i> 3 pp. 99-108 (1980);		
		EN	Muller, G., et al. (1995)"Characterization Of Non-Inducible Tet Repressor Mutants Suggests Conformaional Changes Necessary For Induction", <i>Nature Structural Biology</i> , Vol. 2(8), pp. 693-703;		
		EO	Mullins, L.J. and Mullins, J.J. (1996) "Transgenesis in the Rat and Larger Mammals." J. Clin. Invest. 98(11) Supplement 1996: S37-S40;		
		EP	Murre, C. et al. (1989)"Interactions Between Heterologous Helix-Loop-Helix Proteins Generate Complexes That Bind Specifically to a Common DNA Sequence" <i>Cell</i> 58: 537-544;		
		EQ	Notarianni, et al., (1994)"Production of pharmaceutical proteins from transgenic animals", Journal of Reproduction and Facility, Vol. 41, pp. 51-56;		
Orkin, S. H. and Motulsky, A.G. "Report and recommendations of the panel to assess the investment in research on gene therapy" Dec. 7, 1995.					
Pescini R. et al. (1994) "Inducible Inhibition of Eukaryotic Gene Expression" <i>Biochemical & Biophysical Research Communications</i> 202(3):1664-1667;					
		ET	Pursel et al. "Genetic engineering of livestock" Science 244, pp. 1281-1288 (1989);		
		EU	Renkawitz R. (1990) "Transcriptional Repression In Eukaryotes" <i>TIG</i> 6(6):192-193;		
Salter, et al. "Transgenic chickens: insertion of retroviral genes into the chicken germ lin <i>Virology</i> 157, pp. 236-240 (1987);					
		EW	Sato, K. et al. (1986) "A specific DNA Sequence Controls Termination of Transcription in the Gastrin Gene" <i>Molecular and Cellular Biology</i> 6(4): 1032-1043;		
		EX	Sauer, F. and H. Jäckle (1993) "Dimerization and the Control of Transcription by Krüppel" Nature 364:454-457;		
		EY	Seamark, R.F. (1994) "Progress and Emerging Problems in Livestock Transgenesis: a Summary Perspective." <i>Reprod. Fertil. Dev.</i> 6: 653-657;		
		EZ	Strojek, et al. (1988) "The Use Of Transgenic Animal Techniques For Livestock Improvement", Genetic Engineering, Principles and Methods, Vol 10, pp. 221-246;		
		FA	Wall, R.J., (1996)"Transgenic Livestock:Progress and Prospects For The Future" <i>Theriogenology</i> , Vol. 45, pp. 57-68;		
		FB	Weinmann P. et al. (1994) "A Chimeric Transactivator Allows Tetracycline-Responsive Gene Expression in Whole Plants" <i>The Plant Journal</i> 5(4):559-569;		
		FC	Sizemore, C. et al.(1990)"Quantitative Analysis of Tn10 Tet Repressor Binging To A Complete Set Of <i>Tet</i> Operator Mutants", <i>Nucleic Acids Research</i> , Vol. 18(10), pp. 2875-2880;		
m		FD	Wissmann, A. et al. (1991) "Selection for Tn10 Tet Repressor Binding to tet Operator in Escherichia coli: Isolation of Temperature-Sensitive Mutants and and combinatorial Mutagenesis in the DNA Binding Motif" Genetics 128:225-232;		
			Date Considered 511 N		

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		ICT /	25 D	LIPLICATIONS SITES BY APPLICANT	BBI-013C3CN2	09/281,674	
	LIST OF PUBLICATIONS CITED BY APPLICANT (Use several sheets if necessary)				Bujard, H., Gossen, M., Salfeld, J. and Voss, J.		
	T		皇。		03/30/1999	1643 1632	
100 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0				OTHERS (including Author, Title, I Wissmann, A., et al., (1991)"Amino Acids I	Date, Pertinent Pages, Etc.)	Specificity In The Haliv	
Turn-Helix Motif Of Tn10 Tet Repressor", <i>The EMBO Journal</i> , Vol. 10(13), pp. 4145-4 Yarranton G. (1992) "Inducible Vectors For Expression In Mamalian Cells" <i>Current C</i>					3) pp 4145-4152		
Biotechnology 3:506-511.				Biotechnology 3:506-511.	r Expression in Mamalian Ce	lls" Current Opinion in	
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